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Head and neck cancer in the elderly: A cohort study in 40 patients

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Abstract

Introduction. In the industrialized nations of the Western hemisphere the age group beyond 75 years will grow steadily, requiring special attention by medical professionals in the future. With regard to these expectations 40 patients, beyond the age of 75 and who were first diagnosed to suffer from squamous cell carcinoma of the upper aerodigestive tract, were analysed. *Material and methods*. Forty patients diagnosed and treated between 1998 and 2003 for head and neck squamous cell carcinoma (HNSCC) were analysed. *Results*. Laryngeal carcinoma was noted in 80% of the patients. All types of treatment were tolerated well. Patient compliance was generally good and the rate of complications was low. *Conclusion*. The results of the present study show that HNSCC in elderly patients should be treated with curative intention. Age itself should never be a sole factor in deciding which curative therapy should be undertaken. Exceptions could be made in patients with severe general comorbidity.

Introduction

The increasing life expectancy in the Western industrialized nations is, among other reasons, a result of advanced medical care. Societies will be characterized by an increasing population of elderly citizens, who will require specialized medical care. Diagnostic and therapeutic management of diseases will require an adjustment to the needs of the elderly. The term "elderly age" is not defined exactly in the literature. At the age of 75 years, patients are frequently addressed as old patients [1]. In geriatric medicine the following age groups are distinguished: the group of the so-called younger patients (65–70 years), the group of elderly patients (75–84 years) and eldest patients ($\geq$85 years). Due to the fact that biological age may differ greatly from chronological age, the classification of patients should not only be based on chronological age [1]. In the years to come the group of elderly citizens, especially those beyond the age of 75 years, will be the group with the greatest growth dynamic within societies of the Western industrial nations [2].

Only a few investigations exist on the therapy and prognosis of carcinomas of the upper aerodigestive tract (UADT) in the advanced age patient. One reason for this observation may be the fact that elderly patients are often excluded from clinical investigations because of their age [3–5]. The presented investigation analyses the course of malignant disease of patients who suffered from squamous cell carcinoma (SCC) of the UADT but who were first diagnosed for that disease at the age of 75 or older.

Material and methods

A total number of 40 patients $\geq$75 years of age were analysed during a five-year period (1998–2003). All patients were treated for SCC of the UADT and were followed-up in the oncology clinic of the Department of Otolaryngology, Head and Neck Surgery of the University of Marburg. In fact all patients $\geq$75 years of age who presented to our department for the first time with the above-mentioned diagnosis were included in the present investigation. Exclusion criteria were non-SCC, basal cell carcinoma, or SCC of the skin. The following data were assessed: age, gender, duration of disease, location of the tumour, TNM stage, and pre-therapeutic haemoglobin values. Furthermore, comorbidity was analysed and causes of death of

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deceased patients were evaluated wherever possible. Statistical analysis was performed using a computer with the software package SPSS Version 11.5 (SPSS Inc., Chicago, IL, USA).

Results

The median age of the patients at initial diagnosis of the head and neck SCC was 77 years (range: 75–96 years). Most of the 40 patients were of male gender (38/40; 95%). The median follow-up period was 25 months (range: 3–121). At the conclusion of the investigation 13/40 patients (32.5%) had died. The duration of initial symptoms until presentation to the Department of Otolaryngology was 15.5 (median) weeks (range: 0–208). In 27/40 cases (67.5%) the patients were referred to the hospital by ENT specialists.

Cardiovascular diseases were the most important and at the same time the most common comorbidities, with 40% (16/40) of the patients affected (Table I). Among the second primary tumours bronchial carcinoma could be detected in two cases, two patients suffered from a colon carcinoma, and one patient from a carcinoma of the prostate. A synchronous or metachronous second primary carcinoma of the UADT could not be detected during the investigation period.

According to the ASA classification of the American Society of Anaesthesiology, which estimates the perioperative risk of anaesthesia with regard to the physical constitution of patients, the majority of patients could be classified as ASA stage 2 and 3 (Table II).

The distribution of the primary tumour location in the 40 patients examined is described in Table III. The TNM stages were transferred into the respective UICC stages (Table III). Distant metastases were identified radiologically in 5/40 cases (12.5%) and were all found in the lung. In two patients additional hepatic metastases were diagnosed. These patients had advanced primary tumours with cervical metastases; three of them suffered from supraglottic laryngeal carcinoma (T2N2b; T3N1; T3N2b) as well as one patient with a carcinoma of the tongue (T1N1), and one with a carcinoma of the tonsil (T2N2c). These five patients with distant metastases had no prior tumour history.

Table I. Concomitant diseases.

Disease	No. of patients
Cardiovascular disease	16
Coincident carcinoma—2nd primary cancer	5
Pulmonary disease	4
Diabetes	5
Genitourinary disease	3
Gastrointestinal disease	2
Miscellaneous	6

Table II. ASA classification.

ASA	Physical condition	n
ASA 1	Healthy patient	0
ASA 2	Mild systemic disease, no functional limitation	13
ASA 3	Severe systemic disease, define functional limitation	26
ASA 4	Severe systemic disease that is a constant threat to life	1
ASA 5	Moribund patient unlikely to survive 24 hours with or without surgery	0

The treatment chosen was dependent on tumour size and localization, and was always decided with the patient. Decision-making thus did not vary according to the age of the patients. Half of the patients underwent CO_2 laser surgical resection of the tumour (Table IV). A temporary tracheotomy was necessary in one patient who was initially treated by radiotherapy for T4 laryngeal carcinoma. It was possible for the tracheotomy to be reversed 11 months later. Altogether 11/40 patients were diagnosed by ultrasound to have neck lymph node metastases. In nine of these patients (22.5%) a neck dissection was performed together with the tumour resection. The other two patients had their lymph node metastases in combination with large, primarily non-resectable tumours. These patients received primarily radiochemotherapy.

In 12.5% (5/40) of the patients radiochemotherapy was performed primarily, followed by subsequent surgery. An isolated primary radiotherapy was performed in 10% (4/40). One patient had to abandon therapy because of rapid deterioration. This patient died from cardiovascular failure 18 days later. In one case the initially planned adjuvant radiochemotherapy after CO_2 laser resection of a T2 carcinoma of the tongue was refused. All other cases were inconspicuous.

A merely palliative therapy was performed in only two cases, meaning that palliative radiotherapy was initiated. Two patients developed recurrent malignant disease, which was treated by palliative chemotherapy (methotrexate) in the first case and palliative radiotherapy in the second case (see Table IV).

The median pre-therapeutic haemoglobin level was 14.5 g/l.

The only serious complication occurring was tumour-associated bleeding in two cases of residual tumour after primary radiochemotherapy, which could be managed surgically in both cases. However, both cases developed transient psychosis for a short period of time. These episodes had no severe

Table III. Distribution of primary tumour site.

			Stage of disease				Histological grading		
Primary site	n	%	UICC I	UICC II	UICC III	UICC IV	G1	G2	G3
Larynx	32	80	15	4	5	8	4	23	5
Supraglottic	11	27.5		3	2	6		9	2
Glottic	21	52.5	15	1	3	2	4	14	3
Oral cavity	3	7.5	1	1	1			3	
Oropharynx	3	7.5				3		1	2
Hypopharynx	1	2.5				1			1
Nasal septum	1	2.5		1				1	
Total	40	100%	16	6	6	12	4	28	8

influence on further therapy and could be managed by application of antipsychotic drugs, as recommended by the psychiatrist.

In all, 5% of the patients (2/40) had local recurrences.

Regarding the compliance of the tumour patients it can be said that the fixed appointments for oncological follow-up were kept by 33 of 40 of the patients. Additionally nearly all patients were satisfied with regular oncological follow-up consultation hours on fixed days. Also great spatial distances to the ENT department with the necessity for many hours of travelling did not seem to bother the patients.

At conclusion of the investigation (31 August 2003) 27/40 (67.5%) patients were alive and well. At least 12/13 (92.3%) had died due to the consequences of the tumour disease (tumour cachexia, cervical lymph node or distant metastases, and coincident carcinoma) in cardiovascular arrest; another patient had died from a stroke (Table V). Owing to the low rate of autopsy (2/13) cardiovascular arrest was the major diagnosis for cause of death after necropsy. With regard to the respective UICC stages it became evident that the deceased patients were mostly those who initially suffered from advanced tumour stages (stage III: n = 3; stage IV: n = 6). Survival increased with lower UICC stages and histological grading.

Table IV. Treatment modalities.

Treatment modality	n (%)
CO_2 laser-surgical resection	20 (50)
Conservative tumour resection	1 (2.5)
Laryngectomy	2 (5)
Partial laryngectomy	2 (5)
Neck dissection	9 (22.5)
Tracheostomy	2 (2.5)
(Chemo-) radiotherapy	9 (22.5)
Adjuvant (Chemo-) radiotherapy	2 (5)
Palliative chemotherapy	1 (2.5)
Palliative radiotherapy	3 (7.5)

Discussion

Currently the mean age of initial diagnosis in head and neck cancer is in the sixth decade of life. Recent studies regarding carcinogenesis in ageing patients led to the assumption that a series of spontaneous mutations is responsible for tumour cell transformation rather than an increased exposure to carcinogenic substances [6]. Because of this phenomenon, as well as the ageing process, a hypomethylization of the DNA seems to be a responsible factor for malignant transformation [7,8]. Furthermore it is a well-known fact that increased oncogen activation occurs with ageing of cells and tissue [9].

It should be pointed out again that all of the patients in this study had their first diagnosis of the SCC at the age of 75 or older. Reports published to date regarding neoplasms of the UADT in patients of advanced age [1,3,6,10–22] do not allow satisfactory comparisons. One reason for this observation may be differences in the initial situations of the respective study designs. Differences in the study designs could be identified with regard to the minimum age of the patients, the localization of the tumours, and the definition of disease stages. In the various publications on elderly tumour patients the minimum age of the patients has been defined differently. The age limits vary between 65 years [17] via 70 years [3,10,14,16,23], 75 years [6,20] up to 80 years [11,13]. All these examinations have in common that they focus on epidemiological aspects

Table V. Cause of death.

Cause of death	n
Cardiovascular arrest (also tumour related)	11
Cardiovascular disease	1
Coincident carcinoma	1

or on the therapeutic consequences. Psychosocial aspects seemed to be less interesting, although the psychosocial status of elderly patients in our opinion has a significant impact on the course of the disease. Detailed descriptions of actual courses of the diseases have mostly been omitted in the literature.

In elderly patients the length of their syndrome history is of special interest. The median duration of complaints was 15.5 weeks (range: 0–208) until the examined patients in the evaluated group sought medical advice. Regarding the duration no data can be found in the literature. It may be assumed that the majority of patients first went to their general practitioner to present with their complaints. Initial symptoms such as dysphagia and odynophagia or hoarseness were suspected to be related to common colds and thus were not interpreted correctly as early-warning signals. This lead to initial wait-and-see strategies and thus to a significant loss of time before consulting medical practitioners.

Ageing patients consider several symptoms as normal in the ageing process, e.g. loss of weight, lassitude, infirmity, or tiredness. The elderly generation is not used to discussing the diagnosis of cancer openly. In former times therapeutic options of cure were limited, which might explain the reservations of the elderly regarding the topic of malignant diseases. Problems of the elderly generation such as social isolation due to the loss of partner or friends, the distance to children or other relatives, limited mobility, hearing loss, visual loss, other physical handicaps, or already existing diseases occupy more space in the awareness of the patients than cancerous diseases. An eventual newly developed malignant disease is likely to be suppressed, as long as the symptoms do not influence daily routine.

In elderly patients the distribution of SCC in the UADT shows diverging results. Tumour distribution in the UADT over all age groups, according to the WHO, is as follows: 43% in the oral cavity, 31% in the pharynx, and 26% in the larynx [24]. Similar results were found by Sarini, who examined 273 patients at the age of 75 or older [21]). In 1983 Jun [13] discovered in an examination of 159 patients beyond the age of 80 that 53% of tumours were located in the oral cavity, 10.9% in the larynx, and 5.8% in the pharynx. With regard to the above-mentioned percentages in particular, the results of the present study reflect a completely different distribution. The high number of laryngeal carcinomas (80%) in the patient population evaluated was surprising to us but may possibly be the result of the laser surgical focus of our department. The low percentage of neoplasms in the pharynx and oral cavity is remarkable. The percentage of patients abusing alcohol decreases in the elderly in comparison with tobacco abuse, which could also explain the high percentage of glottic laryngeal carcinomas. A similar observation was made by Koch et al. [6], who showed that the alcohol abuse of elderly cancer patients was significantly lower than that of younger head and neck cancer patients. The present study reveals that in our patient population the distribution of SCC is significantly higher in the larynx for elderly patients compared with younger patient groups from other studies [13,21,24]. As stated by Repetto, elderly patients more frequently present comorbid chronic conditions with functional limitations [25]. In this series concomitant diseases were most often found in the cardiovascular system but concomitant diseases had been treated sufficiently, or at least no grave influences of the course of the malignant disease through inadequately treated concomitant disease could be noted.

The median pre-therapeutic haemoglobin level of 14.5 g/l was satisfying. Dietz [26] reported on a median pretherapeutic Hb level of 13.5 g/l in 125 cancer patients with UICC stage III–IV prior to primary radiochemotherapy. According to Dietz a decrease in haemoglobin levels is a predictive marker for prognosis indicating an unfavourable clinical course of the disease. The patients had a median decrease of haemoglobin values of 1.1g/l. This observation did not seem to affect the patients. According to the WHO, the diagnosis of tumor anaemia should only be made if the haemoglobin level drops below 11 g/dl.

The comparably high rate of radiologically diagnosed distant metastases of 12.5% in this study has to be addressed. Histological proof of these findings was not confirmed in any of the cases so that an exact differentiation of the pulmonary tumours, e.g. bronchial carcinoma, was not possible. The other two patients with additional hepatic distant metastatic spread did not reveal any other neoplasms in the GI tract, which would have been more likely to form hepatic metastases than head and neck cancer. Invasive diagnostic procedures were avoided, because of the absence of clinical symptoms and taking into account the advanced disease.

Regarding the therapeutic options of the patient population examined, surgery was the first choice, provided that the tumour showed limited expansion and access to the tumour was good. In this respect, transoral laser microsurgery of SCC of the UADT played an increasingly important role [27]. Through the endoscopic approach an extensive conventional surgical approach could often be avoided. In particular, the majority of glottic and supraglottic laryngeal carcinomas were resected by means of a CO_2 laser. But also extensive surgical interventions such as free-flap reconstruction are considered as suitable

therapy options in the elderly provided that patients are in good health preoperatively [20].

Perioperative complications were not observed. Five of 40 patients [12.5%] received primary radiochemotherapy for advanced disease, either because they refused surgery or because concomitant secondary disease did not allow surgery under general anaesthesia. Some 10% (4/40) underwent primary radiotherapy. In none of these cases did therapy have to be interrupted. In this context carcinomas of the pharynx that fulfilled the UICC stage IV have to be addressed specifically. Even after initiation of adjuvant radiotherapy (3/40) or radiochemotherapy (2/40) patients showed good compliance, especially when therapy could be performed on an outpatient basis.

Survival rates in similar age groups and similar study designs vary between 16.5% (21) and 43% (14) with regard to five-year survival rate. The results presented show that the average prospective survival rate in this cohort (based on a median age of 77 years) of 45 months diverges from the expected survival rate of healthy persons of similar age. An 80-year-old person, for example, had a life expectancy of a further 8 years and a 70-year-old person had a life expectancy of a further 15 years [28] in the ninth decade of the twentieth century. When linked to tumour status and differentiation of carcinomas the prognosis of patients declined with higher UICC stages and lower stages of tumour differentiation.

In recent years progress in the field of preoperative diagnosis and anaesthesia has resulted in more successful and more aggressive therapeutic strategies for patients suffering from head and neck cancer. Thus even advanced age did not automatically present a contraindication for radical treatment concepts [11,23] because postoperative complications after extended tumour surgery did not occur more often than in younger cancer patients [17]. In order to minimize particularly peri- and postoperative complications close cooperation with the anaesthetist is indispensable for the success of any surgical intervention [1]. Good recovery and quick postoperative mobilization of patients with SCC of the UADT reduces the risk of thromboembolic complications. Disturbances of fluid and electrolyte balances occur only rarely and postoperative pain therapy can be administered well [16]. Causes of death of the patients were predominantly cardiovascular failure and progressive tumour in 12/13 cases. Another patient died as the result of a stroke in another institution. The missing specification of the causes of death is due to a low autopsy rate in the present patient population. Five of 13 patients died in hospital but only in two patients had consent been given for autopsy. In the other cases causes of death had been diagnosed by the general practitioner at necropsy without further information being given.

The existing results underline that curative therapy for SCC of the UADT in ageing patients should be attempted, not only because of the low rate of therapy-associated complications but also because of the comparatively good prognosis. A major proportion of the primary tumours are located in regions that are easily accessible. The treatment of choice should be based on a medical assessment and the preferences of the patient, not on chronological age [4]. A central task in the care of elderly patients with oncological diseases will be to look more closely at the individual needs of the patient. Not only must adequate medical care be ensured but also care of the psychological needs has to be secured. If the closest social network, such as the husband or wife, children, or other family members, is still intact, then they play a crucial role in psychosocial care. The inclusion of these persons in planning of therapy or decision-making cannot be rejected for multiple reasons. Additionally, integrating the family in treatment planning strengthens confidence in the patient–physician relationship.

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